3-11-2019

Fleischner Society Guidelines and Indications for Follow-up of Low Dose Computed Tomography Screening for Lung Cancer

Jenna Arnold

Fleischner Society Guidelines and Indications for Follow-up of Low Dose Computed Tomography Screening for Lung Cancer

Jenna Arnold, RN, CCRN-CSC-CMC, TCRN, sFNP

University of North Dakota

MSN Program: FNP Track

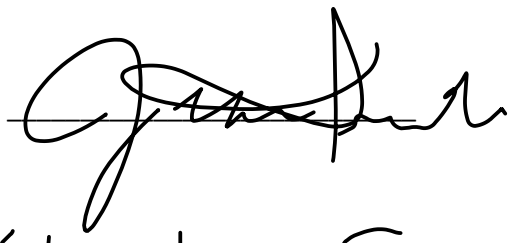
PERMISSION

Title Fleischner Society Guidelines and indications for Follow-up of Low Dose Computed Tomography Screening for Lung Cancer

Department: Nursing

Degree: Master of Science

In presenting this independent study in partial fulfillment of the requirements for a graduate degree from the University of North Dakota, I agree that the College of Nursing & Professional Disciplines of this University shall make it freely available for inspection. I further agree that permission for extensive copying or electronic access for scholarly purposes may be granted by the professor who supervised my independent study work or, in his/her absence, by the chairperson of the department or the dean of the Graduate School. It is understood that any copying or publication or other use of this independent study or part thereof for financial gain shall not be allowed without my written permission. It is also understood that due recognition shall be given to me and to the University of North Dakota in any scholarly use which may be made of any material in my independent study.

Signature 

Date 4-1-19

Abstract

Lung cancer is the leading cause of death associated with malignancy for both men and women in the United States. Lung cancer carries a poor prognosis related to the lack of symptoms early in the course of disease. Sixty-seven percent of lung cancer is not diagnosed until stage III-IV. Screening high-risk populations with low dose computed tomography scans can provide up to 20% decrease in lung cancer mortality. Statistic reveal that 80-90% of all lung cancer diagnoses are associated with tobacco smoking. The case subject of this paper is a 72 year-old Caucasian female with a 45 pack-year cigarette smoking history as well as chronic obstructive pulmonary disease that presented for follow-up after a fall; this patient portrays many high-risk features for lung cancer. The recommended screening population are those age 55-80 with at least a 30 pack-year history of tobacco smoking history. The Fleishner Society has published criteria that should be used as a guideline for follow-up recommendations. All clinicians should be familiar with the Fleishner criteria to improve pulmonary nodule surveillance and, therefore, patient outcomes.

Fleischner Society Guidelines and Indications for Follow-up of Low Dose Computed Tomography Screening for Lung Cancer

Lung cancer is a significant cause of morbidity and mortality in the United States (U.S.), as well as worldwide. It is the leading cause of death associated with malignancy for both men and women in the United States (Azharuddin, Adamo, Malki, & Livornese, 2017). Lung cancers of all types generally carry a poor prognosis, this is largely attributed to the lack of significant symptoms until the disease is advanced; 67.6% are diagnosed in stage III or IV (Ruparel et al., 2016). In fact, the 5-year survival rate in the U.S. is between 12.7(Azharuddin et al., 2017)-18%; this is significant when compared to breast and prostate cancers for which the 5-year survival rate is between 90-100% (Ruparel et al., 2016). The National Cancer Institute has shown that low-dose computed tomography (LDCT) screening reduces lung cancer mortality by 20% (Azharuddin et al., 2017).

LDCT screening for lung cancer has been shown to reduce mortality rates related to lung cancer as discussed above. All patients should be assessed for lung cancer risks and screened appropriately. However, this leads to the detection of many small nodules that may not need intervention; this requires the provider to decide upon further surveillance versus biopsy. The Fleischner Society provides guidelines for clinicians to appropriately follow pulmonary nodules found incidentally or with screening imaging. This paper will discuss the criteria for LDCT screening as well as how to use the Fleischner guidelines for appropriate follow-up.

Case Report

History

A 72-year-old Caucasian, post-menopausal female presented to the clinic for a 6 week follow-up status post fall requiring open reduction internal fixation (ORIF) of right hip fracture. She has no known allergies. She carries a history notable for anemia, hypertension, hypercholesterolemia, current tobacco smoker with 45 pack-year history, bipolar mood disorder, and chronic obstructive pulmonary disease. She denies history of falls, reports that the fall occurred in her home after tripping on a blanket on the floor. Home medications include Fluticasone propionate and salmeterol 250/50 1 puff BID, Prednisone (completed taper), Losartan 50mg PO daily, Metoprolol 50mg PO BID, Paroxetine 20mg PO daily, Quetiapine 200mg PO BID, Lipitor 20mg PO daily, Multivitamin PO daily, and Iron sulfate 325mg PO BID. Immunizations are up to date. She completes recommended colonoscopy screenings and is up-to-date. She has stopped Papanicolaou screenings due to age. She has never been screened for bone density or lung cancer.

She is currently feeling well without complaints. She completed physical therapy last week and is doing well getting around on her own; she has access to a walker for assistance and does still use it occasionally. She denies pain and is only using Tylenol at bedtime. She denies fever, drainage, erythema, induration. She denies numbness, weakness, tingling of right leg. She also recently experienced a flare in her COPD and completed a steroid taper yesterday. She reports that her breathing is back to baseline and denies further concerns. She continues to have mild fatigue. She denies gastrointestinal concerns.

Objective Assessment

Vital Signs: 138/70, 72, 18, 98.6, 92%

General: well-groomed. Appears stated age. No distress.

Neurological: Alert, oriented x4. Strength 5/5 to all extremities.

Cardiovascular: regular rate and rhythm. S1S2 without adventitious sounds. No peripheral edema. Pedal pulses palpable 2+.

Respiratory: Lungs with diffuse scattered rhonchi, clears with cough.
Nonlabored. Nonproductive cough, chronic. Increased AP chest diameter.

Gastrointestinal: soft, nontender, normal contour. Bowel sounds present.

MSK: full ROM and strength 5/5 to bilateral lower extremities.

Integumentary: incision to right hip that is open to air, CDI and edges approximated without erythema, drainage, induration. Skin is warm, dry, without rash noted.

Psych: pleasant. Staying with family members during recovery

Labs/Imaging

BMP: WNL

CBC: WBC 5.8, HGB 11.2, MCV 65, PLT 265

DEXA Scan: T-Score -2.6

Diagnosis and Treatment

Microcytic Anemia. This is likely related to underlying iron-deficiency anemia, coupled with acute blood loss related to recent hip fracture and surgery. Hemoglobin today is 11.2g/dL. Continue to take iron sulfate 325mg BID as tolerated. Plan for recheck hemoglobin at next visit or sooner if symptoms arise.

Osteoporosis. Proven with DEXA scan revealing bone density loss with T-Score -2.6 as well as a recent hip fracture and chronic steroid use. She is high risk for further fractures and I will pursue aggressive treatment. The options and potential side-effects were discussed, she

desires avoidance of injectables. She will be started on a calcium/vitamin D supplement as well as Bisphosphonate therapy with alendronate 10mg oral daily pending dental exam. She was counseled on smoking cessation, alcohol/caffeine limitation, fall prevention strategies, as well as sun safety. She was advised on the importance of weight bearing exercise 150 minutes per week.

Tobacco Dependence. She indicates that she is ready to attempt cessation. She was counseled regarding options and support groups (ND Quits). She will be started on nicotine replacement therapy via nicotine patch releasing 21mg nicotine per day. An appointment will also be set up with our tobacco cessation counselor. She will receive pneumococcal vaccination today. It was discussed that she also meets criteria for lung cancer screening via LDCT.

She will follow-up in 3 months for routine physical with fasting labs or sooner if concerns arise.

Literature Review

This patient portrays the perfect candidate for low-dose computed tomography screening for lung cancer. She is an active 72 year-old female with a 43 pack-year smoking history, this places her at high risk for lung cancer.

A literature review was completed utilizing the PubMed and CINAHL databases. Keyword search terms included “LDCT Indications”, “lung cancer screening”, “Fleischner Criteria”, and “Management of pulmonary nodules”. The results were limited to articles published from 2013-2019. This found 12 articles for inclusion in this paper.

History of Screening

Screening for asymptomatic lung cancer is not a new practice, in fact studies for lung cancer screening began in the 1950s using photofluorograms. Unfortunately, large studies completed in the 1970s-1980s revealed that lung cancer screening with XRay failed to have a mortality benefit. The Prostate, Lung, Colorectal and Ovarian (PLCO) study was a large study of 155, 000 smokers and non-smokers aged 55-74 that were randomized to annual chest Xray or no screening; this study confirmed that there was no effect on lung cancer incidence or mortality by screening with XRay (Ruparel et al., 2015).

In 1999 the Mayo Lung Project completed a pilot study of low-dose computed tomography screening showing that this detected pulmonary nodules in 74% and lung cancer in 4% of those screened; this proved that LDCT screening could detect early-stage lung cancers, however it did not have a benefit on overall mortality and had a significant false-positive rate. This led to the concept to be largely rejected due to the cost and risk of complications related to the false-positive rates (Ruparel et al, 2015).

The concept of lung cancer screening was again explored by the Early Lung Cancer Action Project. The Early Lung Cancer Action Project was a study with 1000 asymptomatic patients aged 60 or older with at least 10 pack-years smoking history. The criteria for a 'positive' nodule was increased to 5mm or larger (Henschke et al., 1999). This new criterion led to 13% of the population having positive baseline scans and 9.7% of those people having early-stage lung cancer. These patients had a 10-year survival rate of 88%. This study changed the perception on lung cancer screening and made it apparent that protocols were needed to

optimize the benefit of screening. The benefits were again reported with the pivotal National Lung Screening Trial (NLST) that compared chest XRay to LDCT in 53,454 smokers and former smokers aged 55-74 (Ruparel et al., 2015).

In 2005, the Fleischner Society published guidelines in response to the growing problem of how to handle solid pulmonary nodules noted on computed tomography scans. The Fleischner Society published separate guidelines for subsolid nodules in 2013. The guidelines were recently revised in 2017 with the solid and subsolid nodule management combined into one simplified table. The Fleischner guidelines are the most referenced protocol for management of pulmonary nodules and incorporate opinions of pulmonologists, surgeons, thoracic radiologists, pathologists, and other specialists for the most comprehensive management recommendations (MacMahon et al., 2017).

LDCT Screening

Indications. The United States Preventative Services Task Force (USPSTF) revised the recommendations regarding lung cancer screening in 2013. The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults age 55-80 years with a 30 pack-year smoking history whom continue to smoke or have quit within the last 15 years. It is recommended that screening be discontinued once a health issue develops that limits life expectancy or the willingness or ability to have surgery. These recommendations mirror the opinions of the American Cancer Society, American Lung Association, American Thoracic Society, American College of Chest Physicians, and the International Association for the Study of

Lung Cancer. All parties stress the importance of involving the patient in discussion of screening and possibility further indicated procedures (Tanoue, Tanner, Could, & Silvestri, 2014).

Benefit. The benefit of LDCT screening is finding lung cancer in stage I, when curative treatment can be sought and successful. Screening is beneficial for lung cancer because of the lengthy asymptomatic phase, this delays symptom investigation until the disease is already advanced. There is an accepted high-risk group (tobacco smokers) to allow screening to be adequately targeted; smoking, tobacco and environmental, account for approx. 80-90% of all lung cancers. Studies have shown that LDCT screening reduces mortality by about 20% (Tanoue et al., 2014).

Smoking Cessation. The impact of screening on smoking cessation remains inconclusive, however, many studies have reported increased smoking cessation in screening participants compared to background population. Smoking abstinence in combination with LDCT screening has been reported to double the reduction of lung cancer mortality compared with screening only (Ruparel et al., 2016). The Centers for Medicare and Medicaid Services policy requires that smoking cessation counseling be done along with the LDCT screening (Mazzone et al., 2018).

Potential Harms. There are multiple potential harms that can occur as a result of screening and should be adequately weighed against potential benefit for each patient. The potential harms should be part of the pre-screening discussion.

Radiation Exposure. The cumulative radiation dosage should be taken in to consideration. It is estimated that the average radiation dose after 10 years is between 9.3-13 millisieverts. An abdominal computed tomography scan repeated with and without contrast is

approximately 20 millisieverts; this is equivalent to about seven years of natural background radiation. It was also estimated that for every 108 lung cancers caught with LDCT screening, 1 major cancer would be induced by radiation (Tanoue et al., 2014).

Overdiagnosis. There is always a risk of finding a cancer that may have been better unfound, or rather, that the cancer would have had no clinical significance if it had not been noted on screening. The diagnosis of lung cancer on screening causes further diagnostic testing, procedures, costs, morbidity, and patient distress. Studies have estimated the overdiagnosis rate of LDCT screening to be between 13-27%, however further long-term follow-up is needed (Tanoue et al., 2014).

Emotional Distress. A positive test result can produce intense psychological distress in the patient, as well as anxiety can be experienced leading up to the annual screening. LDCT screening has been known to have a high false-positive rate, however most false positive results are resolved with further imaging. In the National Lung Screening Trial, of the abnormal scans 96% were false-positives and did not lead to a diagnosis of lung cancer. The false-positive results can lead to further imaging, invasive procedures, as well as psychological distress for the patient (Tanoue et al., 2014).

Fleischner Criteria

As discussed above, the Fleischner Society guidelines are the most widely referenced protocol for the management of small pulmonary nodules. The initial guidelines were published in 2005, with the most recent revision occurring in 2017.

The 2017 revision of the guidelines combined the protocol for solid and subsolid nodules into one table for ease of reference. The recommended follow-up is determined based upon the size of the nodule, presence of multiple nodules, malignancy risk, and nodule make-up (solid or subsolid).

A: Solid Nodules*

	Size			
Nodule Type	<6 mm (<100 mm³)	6–8 mm (100–250 mm³)	>8 mm (>250 mm³)	Comments
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
Multiple				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).

B: Subsolid Nodules*

	Size		
Nodule Type	<6 mm (<100 mm³)	≥6 mm (>100 mm³)	Comments
Single			
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C)
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

(MacMahon et al., 2017)

The revised Fleischner criteria increased the threshold for which follow-up imaging was recommended. This will cut down on un-necessary screenings. The updated guidelines now suggest follow-up for nodules 6mm or larger (prior recommendation was 4mm), unless multiple subsolid nodules are present. The Fleischner criteria leave judgment with the clinician for high-risk patients with a nodule less than 6mm with an optional follow-up in 12 months.

High Risk Features. The Fleischner Society guidelines separate the follow-up recommendations based upon low risk and high risk for lung cancer as well as nodule size. Nodule size and morphology are the main factors that determine malignancy risk. Malignancy risk has been shown to correlate directly with nodule size: 0-1% risk for nodules <5mm, 6-28% risk for nodules 5-10mm, and 64-82% risk for nodules >20mm (Azharuddin et al., 2017). The clinician should also take into consideration high risk patient characteristics such as smoking, exposure to other carcinogens (radon, asbestos, farming), family history of lung cancer, upper lobe nodule location, age, sex, and prior pulmonary history. The intermediate-high risk categories correspond to an estimated cancer risk of 5-65%. High risk features include older age, heavy smoking history, larger nodule size, spiculated margins, and upper lobe location (MacMahon et al., 2017). Research supports that nodules located in the upper lobes are more likely to be malignant and nodules located along the fissure have low risk of malignancy (McWilliams et al., 2013). If there are multiple nodules noted on imaging, recommendations should be followed for the largest, most suspicious nodule (MacMahon et al., 2017). Decision regarding follow-up should always be personalized to the specific patient and their risk factors for malignancy (Hostetter et al., 2017).

Tissue Sampling. The Fleischner Society guidelines do not give specific recommendations regarding the appropriate time for tissue sampling. The Fleischner criteria only provide guidelines regarding noninvasive monitoring of lung nodules. The clinician should pursue further work-up of nodules in high-risk patients with suspicious nodules, nodules >8mm in size, or rapidly growing nodules. In 2014, the American College of Radiology published additional guidelines based largely upon the Fleischner criteria; the Lung-RADS protocol is specific to LDCT lung cancer screening and provides follow-up imaging recommendations as well as when to pursue biopsy.

Category	Category Descriptor	Category	Findings	Management	Probability of Malignancy	Estimated Population Prevalence
Incomplete	-	0	prior chest CT examination(s) being located for comparison part or all of lungs cannot be evaluated	Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed	n/a	1%
Negative	No nodules and definitely benign nodules	1	no lung nodules nodule(s) with specific calcifications: complete, central, popcorn, concentric rings and fat containing nodules	Continue annual screening with LDCT in 12 months	< 1%	90%
Benign Appearance or Behavior	Nodules with a very low likelihood of becoming a clinically active cancer due to size or lack of growth	2	solid nodule(s): < 6 mm new < 4 mm part solid nodule(s): < 6 mm total diameter on baseline screening non solid nodule(s) (GGN): < 20 mm OR ≥ 20 mm and unchanged or slowly growing category 3 or 4 nodules unchanged for ≥ 3 months			
Probably Benign	Probably benign finding(s) - short term follow up suggested; includes nodules with a low likelihood of becoming a clinically active cancer	3	solid nodule(s): ≥ 6 to < 8 mm at baseline OR new 4 mm to < 6 mm part solid nodule(s) ≥ 6 mm total diameter with solid component < 6 mm OR new < 6 mm total diameter non solid nodule(s) (GGN) ≥ 20 mm on baseline CT or new	6 month LDCT	1-2%	5%
Suspicious	Findings for which additional diagnostic testing and/or tissue sampling is recommended	4A	solid nodule(s): ≥ 8 to < 15 mm at baseline OR growing < 8 mm OR new 6 to < 8 mm part solid nodule(s: ≥ 6 mm with solid component ≥ 6 mm to < 8 mm OR with a new or growing < 4 mm solid component endobronchial nodule	3 month LDCT; PET/CT may be used when there is a ≥ 8 mm solid component	5-15%	2%
		4B	solid nodule(s) ≥ 15 mm OR new or growing, and ≥ 8 mm part solid nodule(s) with: a solid component ≥ 8 mm OR a new or growing ≥ 4 mm solid component	chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a ≥ 8 mm solid component.	> 15%	2%
		4X	Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy			
Other	Clinically Significant or Potentially Clinically Significant Findings (non lung cancer)	S	modifier - may add on to category 0-4 coding	As appropriate to the specific finding	n/a	10%
Prior Lung Cancer	Modifier for patients with a prior diagnosis of lung cancer who return to screening	C	modifier - may add on to category 0-4 coding	-	-	-

(Martin, Kanne, Broderick, Kazerooni, & Meyer, 2017)

Adherence. While the Fleishner guidelines are the most referenced incidental pulmonary nodule management guidelines, they are not universally followed. There is radiologist and clinician deviation in real-world practice. A study reviewed 1,432 radiology reports from the years 2008-2010 and found that adherence to the Fleischner criteria was only done about 57% of the time for the initial scan. The main theme was deviation toward over-management of incidental nodules. If follow-up was recommended, the adherence rate increased with subsequent scans with 79% adherence to Fleischner guidelines on the fourth scan (Masciocchi, Wagner, & Lloyd, 2012). It has been reported that adherence regarding follow-up can be improved by including the Fleischner Society guidelines on the radiology report. However, this takes extra time for the reading radiologist to review the patient co-morbidities and malignancy risks (McDonald et al., 2017).

Summary

Lung cancer screening with LDCT scan reduces mortality related to lung cancer by 20%, however appropriate candidate selection is important. Follow-up of nodules should take into consideration patient malignancy risk as well as nodule characteristics. All clinicians responsible for ordering computed tomography scans should make themselves familiar with management guidelines, whether that is the Fleishcner guidelines or the lung-RADS, for improved patient outcomes.

Learning Points

- Appropriate use of LDCT screening can reduce lung cancer mortality by 20%
- LDCT screening has been shown to be a highly sensitive tool to diagnose early lung cancer
- Candidates for LDCT screening: age 55-80 with 30 pack-year smoking history
    - currently smoking or quit within the last 15 years
- Pulmonary Nodules should be followed using the Fleischner or lung-RADS criteria
- High risk features:
    - Older age
    - Upper lobe nodule location
    - Spiculated mass
    - Significant smoking or carcinogen exposure
    - Family history of lung cancer
    - Presence of other pulmonary conditions
- Fleischner criteria were revised in 2013:
    - Follow-up required for solid nodules >6mm (instead of 4mm)

References

Azharuddin, M., Adamo, N., Malik, A., Livornese, D. (2017). Evaluating pulmonary nodules to detect lung cancer: Does Fleischner criteria really work? *Journal of Cancer Research and Practice*, 1-7.

Callister, M. (2017). The Fleischner guideline. *Journal of Thoracic Oncology, 12*(1152)

Henskchke, C., McCauley, D., Yankelevitz, D., Naidich, D., McGuinness, G., et al. (1999). Early lung cancer action project: overall design and findings from baseline screening. *Lancet, 354*(9173), 99-105.

Hostetter, J., Morrison, J., Morris, M., Jeudy, J., Wang, K., Siegel, E. (2017). Personalizing lung cancer risk prediction and imaging follow-up recommendations using the National Lung Screening Trial dataset. *Journal of the American Medical Informatics Association, 24*(6), 1046-1051

MacMahon, H., Naidich, D., Goo, J., Lee, K., Leung, A., Mayo, J., Mehta, A. et al. (2017). Guidelines for management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. *Radiology, 284*(1), https://doiorg.ezproxylr.med.und.edu/10.1148/radiol.2017161659

Martin, M., Kanne, J., Broderick, L., Kazerooni, E., Meyer, C. (2017). Lung-RADS: Pushing the limits. *RadioGraphics, 37*(7), https://doi.org/10.1148/rg.2017170051

Masciocchi, M., Wagner, B., Lloyd, B. (2012). Quality review: Fleischner criteria adherence by radiologists in a large community hospital. *Journal of the American College of Radiology, 9*(5), 336-339.

Mazzone, P., Silvestri, G., Patel, S., Kanne, J., Kinsinger, L., Weiner, R., Hoo, G., Detterbeck, F. (2018). Screening for lung cancer. *Chest Journal, 153*(4), 954-985.

McDonald, J., Koo, C., White, D., Hartman, T., Bender, C., Sykes, A. (2017). Addition of the Fleischner Society guidelines to chest CT examination interpretive reports improves adherence to recommended follow-up care for incidental pulmonary nodules. *Academic Radiology, 24*(3), 337-344.

McWilliams, A., Tammemagi, M., Mayo, J., Roberts, H., Liu, G. et al. (2013). Probability of cancer in pulmonary nodules detected on first screening CT. *The New England Journal of Medicine, 369*(10), 910-919.

Ruparel, M., Quaife, S., Navani, N., Wardle, J., Janes, S., Baldwin, D.(2016). Pulmonary nodules and CT screening: the past, present, and future. *Thorax, 71(*4), 367-375.

Tanoue, L., Tanner, N., Gould, M., Silvestri, G. (2015). Lung cancer screening. *American Journal of Respiratory and Critical Care Medicine, 191(*1), 19-33.